Pulmonary vasculitis associated with cholangiocarcinoma of liver

E.L.C. Ong, S. Evans and S.P. Hanley

Department of Chest Diseases, Monsall Hospital, Newton Heath, Manchester M10 8WR, UK.

Summary: A 62 year old woman presented with an acute pulmonary vasculitis which responded to treatment with oral steroids. Investigations over one year revealed a cholangiocarcinoma of the liver. The association of vasculitis with neoplastic diseases remains a diagnostic challenge.

Introduction

Cutaneous and systemic vasculitides are well recognized to occur in association with neoplastic disease such as lymphoproliferative disorders, melanoma and renal cell carcinoma, and may precede their diagnosis by up to 6 years. 1-7 We report a previously unrecorded association between an acute steroid responsive pulmonary vasculitis and the finding of an hepatic cholangiocarcinoma one year later.

Case report

A previously fit 62 year old Caucasian dental receptionist presented in June 1987 with a 10 day history of pyrexia, malaise and progressive dyspnoea. She had smoked for a total of 30 pack years, and had a history of allergy to nickel. She had received her first dose of hepatitis B vaccine (Hep-vax, a plasma-derived vaccine) three months previously, and oral ampicillin for 5 days prior to presentation. On examination, she was febrile (39.5°C), and tachypnoeic. Her pulse was 90/minute, in sinus rhythm, jugular venous pressure was elevated at 3 cm, and blood pressure was 120/70 mmHg. On auscultation a third heart sound was present with a short systolic murmur heard over the whole precordium. There were widespread bilateral inspiratory crackles over both lung fields.

Investigations: haemoglobin 11.2 g/dl, white cell count 23.0 x 10⁹/l (91% neutrophils 7% lymphocytes 1% monocytes, 1% eosinophils), plasma viscosity 2.08 cP (normal 1.50–1.72), sodium 129 mmol/l, potassium 3.6 mmol/l, chloride 90 mmol/l, bicarbonate 29 mmol/l, creatinine 109 μmol/l, urea 9.8 mmol/l, albumin 23, total bilirubin 14 μmol/l, alkaline phosphatase 293 IU/l (normal 35–105), aspartate transaminase 137 IU/l (normal 0–35), alanine transaminase 53 IU/l (normal 0–35), gamma glutamyltransferase 210 IU/l (normal 0–30). The arterial blood gas sampling on air showed pH 7.42 (7.36–7.45), PCO₂ 35.5 mmHg (35–45), PO₂ 65.8 mmHg (85–105). A chest radiograph (Figure 1) showed marked interstitial shad-owing in both lungs. The 12-lead electrocardiograph showed no acute changes. Autoantibody screen was negative. Immunoglobin levels were normal. Hepatitis B core antibody was negative. Paired serology for Mycoplasma pneumoniae, Legionella pneumophila and Chlamydia psittaci was unremarkable.

An initial diagnosis of pulmonary oedema was made but when she did not respond with frusmide, ampicillin and erythromycin were added. After 48 hours she developed a generalized tender maculo-
papular rash, considered to be a drug-induced rash, and became more dyspnoeic. Repeat chest radiographs showed worsening of the interstitial shadowing. Bronchoscopy and transbronchial biopsy was performed. Microscopy and culture of bronchoalveolar lavage fluid, and histology of the lung biopsies were normal. Abdominal ultrasound including the liver was normal. She continued to deteriorate and an open lung biopsy was eventually undertaken, the histology (Figure 2) of which showed a vasculitic picture; subsequent section and review of the transbronchial biopsy revealed similar changes. On starting treatment with prednisolone with an initial dose of 60 mg/day she improved rapidly and was discharged home.

Figure 2 Lung tissue showing vasculitis involving medium sized arteries. These vessels showed marked intimal fibrosis and infiltrate with acute and chronic inflammatory cells. (H & E x 75)

On subsequent review whilst on a maintenance dose of prednisolone reduced to 12.5 mg/day, fluctuating liver function tests were noted with the alkaline phosphatase varying from 88 to 220 IU/l, gamma glutamyl transferase from 130 to 226 IU/l and alanine transaminase from 8 to 35 IU/l. Repeat blood counts showed a persistent macrocytosis with a normal vitamin B12 and folate, and unremarkable marrow aspirate. Lung function tests showed a restrictive pattern with progressive improvement but the diffusion never improved to more than 55% of predicted. Her chest radiograph returned to normal. Clinically she maintained her improvement except for an episode of herpes zoster affecting the right sacral 1st

Figure 3 Liver tissue showing cholangiocarcinoma with severe steatosis. (H. & E. x 45)

It is interesting to speculate whether the hepatitis B vaccination could have immunologically unmasked the underlying malignancy by manifesting itself as a vasculitis. The vaccine itself is not known to cause vasculitis; however, a possible association between influenza vaccination and small-vessel vasculitis had been previously documented.9

Recognition of the association between certain vasculitic syndromes and neoplastic diseases remains a diagnostic challenge, we suggest that such cases be closely monitored and investigated as appropriate if no apparent causes are found in the initial onset of the illness.

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